

AMENDMENTS TO THE CLAIMS

1.-32. (Cancelled)

33. (Currently amended) A method for detecting the presence of a target nucleic acid in a sample comprising:

treating a sample containing nucleic acid with an agent that modifies unmethylated cytosine;
providing to the treated sample a detector ligand in the form of an intercalating nucleic acid (INA) capable of binding to a target region of nucleic acid, and allowing sufficient time for the INA detector ligand to bind to the target nucleic acid; and

detecting binding of the INA detector ligand to the target nucleic acid ~~molecule in the sample~~ to indicate the presence of the target nucleic acid in the sample.

34. (Previously presented) The method according to claim 33 wherein the nucleic acid is obtained from a genome of an eukaryote, a prokaryote, virus, mitochondrial nucleic acid, nucleic acid found in other cellular organelles, extracellular nucleic acid, DNA and RNA forms and natural or artificial derivatives of DNA and RNA.

35. (Previously presented) The method according to claim 34 wherein the natural or artificial derivatives of DNA and RNA are selected from the group consisting of INA, ANA, MNA, PNA, LNA, HNA, CNA, and chimeric combinations thereof.

36. (Previously presented) The method according to claim 34 wherein the nucleic acid is genomic DNA.

37. (Previously presented) The method according to claim 33 wherein the agent is selected from bisulfite, acetate or citrate.

38. (Previously presented) The method according to claim 5 wherein the agent is sodium bisulfite, a reagent, which in the presence of water, modifies cytosine into uracil.

39. (Previously presented) The method according to claim 33 wherein the INA is phosphoramidite of (S)-1-O-(4,4'-dimethoxytriphenylmethyl)-3-O-(1-pyrenylmethyl)-glycerol.

40. (Previously presented) The method according to claim 33 wherein the target region includes at least one 5'-methyl cytosine in the untreated nucleic acid.

41. (Previously presented) The method according to claim 33 wherein the detector ligand is directed to a CpG- or CpNpG-- containing region of DNA, where N designates any one of the four possible bases A, T, C, or G.

42. (Previously presented) The method according to claim 41 wherein the CpG-, or CpNpG- containing region of DNA is in a regulatory region of a gene or an enhancer of any regulatory element or region

including promoter, enhancer, oncogene, retro-element, mobile or mobilisable sequence or other regulatory element which activity is altered by environmental factors including chemicals, toxins, drugs, radiation, synthetic or natural compounds and microorganisms or other infectious agents such as viruses, bacteria, fungi and prions.

43. (Previously presented) The method according to claim 33 wherein prior to treating the sample, the nucleic acid is undergoes an enrichment or selection step.
44. (Currently amended) The method according to claim 42 ~~43~~ wherein the enrichment or selection step is selected from the group consisting of physical methods including sonication and shearing, enzymatic digestion, enzymatic treatment, restriction digestion, nuclease treatment, Dnase treatment, concentration, antibody capture, chemical methods including acidic or base digestion and combinations thereof.
45. (Previously presented) The method according to claim 43 wherein the enrichment or selection step is treatment with an antibody directed to 5'-methyl cytosine so as to obtain a methylated nucleic acid sample.
46. (Previously presented) The method according to claim 33 wherein the method detects methylation of a target nucleic acid by providing to the treated sample a detector ligand in the form of an intercalating nucleic acid (INA) capable of distinguishing between methylated and unmethylated cytosine of nucleic acid, such that detection of binding of the detector ligand to the nucleic acid in the sample is indicative of the extent of methylation of the target nucleic acid.
47. (Previously presented) The method according to claim 33 wherein a capture ligand capable of recognising a first part of a target nucleic acid sequence is bound to a solid support such that the treated nucleic acid binds to the support via the first capture ligand, the bound nucleic acid is then exposed to a detector ligand capable of recognising a second part of the target nucleic acid sequence and allowing sufficient time for the detector ligand to bind to a target nucleic acid bound to a support wherein binding of the detector ligand to nucleic acid bound to the support is measured to determine the presence of the target nucleic acid in the sample, wherein at least one of the capture ligand or the detector ligand is an INA ligand.
48. (Previously presented) The method according to claim 47 wherein the ligands are selected from the group consisting of INA probe, peptide nucleic acid (PNA) probe, LNA probe, HNA probe, ANA probe, MNA probe, oligonucleotide, modified oligonucleotide, single stranded DNA, RNA, aptamer, antibody, protein, peptide, a combination thereof, and chimeric versions thereof.

49. (Previously presented) The method according to claim 48 wherein the capture ligand is selected from the group consisting of INA probe, PNA probe, and oligonucleotide probe.
50. (Previously presented) The method according to claim 15 wherein both the capture ligand and the detector ligand are an INA ligand.
51. (Previously presented) The method according to claim 47 wherein the detector ligand is an INA ligand capable of distinguishing between methylated and unmethylated cytosine of DNA and the degree or amount of binding of the detector ligand is indicative of the extent of methylation of the target nucleic acid.
52. (Previously presented) The method according to claim 47 wherein the support is selected from the group consisting of plastic materials, fluorescent beads, magnetic beads, shaped particles, plates, microtiter plates, synthetic or natural membranes, latex beads, polystyrene, column supports, glass beads or slides, nanotubes, arrays, fibres, organic, and inorganic supports.
53. (Previously presented) The method according to claim 52 wherein the support is a magnetic bead, a fluorescent bead, a shaped particle, bead array, or a microtiter plate with one or more wells.
54. (Previously presented) The method according to claim 47 wherein a plurality of capture ligands are arrayed on the solid support.
55. (Previously presented) The method according to claim 33 wherein the INA detector ligand has a detectable label attached thereto.
56. (Previously presented) The method according to claim 55 wherein detectable label is selected from the group consisting of chemiluminescence, fluorescence, radioactivity, enzyme, hapten, and dendrimer.
57. (Previously presented) The method according to claim 33 wherein the nucleic acid bound to the INA detector ligand is further processed or treated.
58. (Previously presented) The method according to claim 57 wherein the nucleic acid is amplified using polymerase chain reaction using primers directed to regions of nucleic acid.
59. (Previously presented) The method according to claim 58 wherein the primers are INA ligands.
- 60-64. (Withdrawn)